Implementation of the "Vascular Age Index" for the interpretation of applanation tonometry

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Summary

Background The application of pulse wave analysis in clinical practice is significantly limited due to the difficulties with evaluation of obtained data. The aim of the study was to propose the new index named "Vascular Age Index" for the improvement and simplification of pulse wave analysis.

Material and methods We examined male and female persons aged from 25 to 76. 128 normotensive participants (the control group, CG) and 150 patients with essential hypertension (EH) were subdivided into subgroups of 25–44, 45–64 and 65 or more years. Each of them included 50 patients. The exception was the oldest subgroup of CG consisting of 28 persons. All participants underwent office blood pressure measurement by automatic blood pressure monitor "Omron 3" and pulse wave analysis carried out with «Sphygmocor XCEL» equipment (AtCor Medical, Australia). Besides common parameters of pulse wave such as augmentation index (AIx) and pulse wave velocity (PWV) the new indicator — "Vascular Age Index" was determined in all persons by the formula: VAI (year)= PWV × AIx ÷ 20.

Results All studied parameters of pulse wave showed strong relationship with age, but the relationship of VAI with age was superior in its strength and significance. It was especially strong ($r = 0.90$; $p < 0.001$) in normotensive patients. The values of VAI obtained in subjects of the control group were approaching to the calendar age, and in patients with hypertension — often exceeded it.

Conclusions Our data confirmed the relationship between AIx and PWV on the one hand, and age and blood pressure on the other. It was shown that in patients of 25–44 years pathological changes of central pulse wave parameters could serve as an additional argument for the diagnosis of hypertension. VAI significantly simplifies the interpretation of central pulse wave study and increases the compliance. Moreover, the diagnostic accuracy of VAI application is rather high. Thus, the implementation of VAI in the routine practice may be recommended.

key words: applanation tonometry, pulse wave analysis, vascular age index

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Background

In recent years the studies of stiffness of blood vessels, particularly of the aorta, turned to have great importance. There are strong evidences of the influence of vessels stiffness on the prognosis in patients with arterial hypertension, coronary heart disease, diabetes, heart failure. Technological advances contributed to the widespread of aortic wall stiffness measurement and allowed to get reasonably accurate values of the pulse wave parameters in aorta on the basis of peripheral arteries noninvasive examination.

The augmentation index and pulse wave velocity are the most discussed in the scientific literature, although the list of parameters defined by applanation tonometry is long. Age and blood pressure were found to have the greatest impact on them. It opens

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the way to the development of equations that accurately predict the values of pulse wave velocity [1] and augmentation index [2]. As a result, the reference values of the central pulse wave for many ethnic groups in Europe such as the Dutch, French, Danes, Britons, Belgians, Greeks, Czechs and Italians were obtained. Similar but smaller-scale studies had been conducted in China, Africa and Malaysia. However, the complexity of application limits the practical use of these regression equations. Therefore, the aim of this study was to simplify the clinical use of applanation tonometry through the using of the new index tentatively called "Vascular Age Index".

Material and methods

Males and females aged 25 to 76 years were involved into the study. According to the clinical examination, they were divided into two groups: the group with essential hypertension (EH) consisted of 150 hypertensive patients and the control group (CG) presented by 128 individuals with normal blood pressure and without history of hypertension. Both groups were divided into subgroups of 25–44, 45–64 and 65 or more years. Each of them included 50 patients with the exception of the oldest subgroup of CG consisting of 28 persons. The study was approved by the local ethic committee. All patients gave their informed consent for the participation in the study. During the period from August to November, 2013, all consequent patients, who met inclusion-exclusion criteria and gave their informed consent, were involved in our study. Inclusion criteria were as follows: males and females aged 25 or more with essential hypertension or without history of arterial hypertension. Exclusion criteria were as follows:

— congenital or acquired heart defects;
— systemic connective tissue diseases;
— endocrine diseases excluding diabetes mellitus;
— type 1 diabetes mellitus (DM) or uncontrolled type 2 DM;
— chronic kidney diseases;
— symptomatic arterial hypertension;
— myocardiopathies of any genesis;
— pulmonary hypertension;
— hemodynamically significant arrhythmias including persistent AF, atrioventricular or sinoatrial blocks of the II–III degree;
— unstable stenocardia at the day of involvement.

General clinical examination and three-fold measurements of systolic and diastolic blood pressure (SBP and DBP, respectively) with an automatic blood pressure monitor Omron M3 were obligate. Pulse wave curve of the radial artery was obtained with Hi-Fi applanation probe and then the aortic pulse wave curve generated automatically.

We obtained such parameters:

Aix (P2 / P1) — augmentation index calculated by the formula:

$$AIx = (100 \times (P2–Pd)) / (P1–Pd) \quad (1)$$

wherein:

Pd — end-diastolic pressure, P1 — end-systolic pressure, P2 — pressure augmentation wave height.

AIx (AP / PP) — augmentation index calculated as the ratio of augmentation pressure to pulse pressure at the end of ventricular systole.

AIx75 — augmentation index calculated by the previous formula, but standardized to the heart rate of 75 per minute.

CESBP — central end-systolic blood pressure.

CSBP — central systolic blood pressure.

CDBP — central diastolic blood pressure.

PPA — pulse pressure augmentation. It is calculated by the formula:

$$PPA = (SBP–DBP) / (CSBP–CDBP)$$

Then we determined pulse wave velocity (PWV) in the carotid-femoral segment of aorta. The distances between the best pulsations of carotid and femoral arteries and sternal notch were measured by measuring tape. Pulse waves (synchronized with the ECG) were consequently recorded at these points. Knowing the length of the carotid-femoral arterial segments and the carotid-femoral delay of pulsations, the pulse wave velocity (PWV) was calculated.

Besides routine pulse wave measurements, we calculated "Vascular Age Index" (VAI). We hypothesize that this index correlates with the biological age of vessels. In healthy individuals it is less or near calendar age. In hypertensive subjects it is significantly higher than their calendar age.

Statistical methods

All values are presented as mean (SD). Non-parametric methods for related and unrelated samples were used to compare the results. Simple regression method was used to obtain the correlation coefficients between the studied parameters of the central pulse wave and peripheral blood pressure values. Statistical processing was performed using the application «Statistica 8.0».

Results

Augmentation index and pulse wave velocity were measured in the hypertensive and control groups. The average values obtained for each age group are shown below (Table I).

Table I. Values of AIx and PWV obtained in normotensive and hypertensive patients

Pulse wave parameters in the age subgroups of CG			
Parameters	**25–44**	**45–64**	**> 65**
AIx (AP/PP)	7.0 (8.2)	22.6 (8.0)	35.5 (12.6)#
AIx (P2/P1)	111.0 (17.0)	130.8 (14.9)	154.5 (25.2)#
AIx75	3.6 (8.6)	16.8 (9.0)	23.0 (8.9)#
PWV	5.3 (0.9)	7.6 (1.4)	9.1 (2.4)#
Pulse wave parameters in the age subgroups of CG			
Parameters	25–44	45–64	> 65
AIx (AP/PP)	24.3 (9.3)*	23.6 (11.0)	32.2 (11.1)#
AIx (P2/P1)	133.8 (16.7)	134.7 (22.7)	152.7 (24.8)#
AIx75	26.2 (8.5)*	19.8 (9.2)	28.5 (10.7)#
PWV	7.7 (1.2)*	8.6 (2.5)	11.0 (2.8)#

*significant differences between the age subgroups of hypertensive patients and normotensive patients

#significant differences between the performance of different age subgroups within the group

Table II. The values of correlation coefficients between AIx75, PWV, VAI and age, SBP, DBP, and MAP

Correlations for AIx75						
Parameters	**CG**	**p**	**EH**	**p**	**Both**	**p**
Age	0.71	0.02	0.15	0.37	0.45	0.002
SBP	0.46	0.25	0.03	0.8	0.30	0.04
DBP	0.57	0.15	–0.08	0.66	0.18	0.2
MAP	0.57	0.08	–0.03	0.8	0.25	0.09
Correlations for PWV						
Parameters	CG	p	EH	p	Both	p
Age	0.85	0.0002	0.51	0.0002	0.6	0.0001
SBP	0.37	0.29	0.34	0.05	0.46	0.002
DBP	0.44	0.20	0.05	0.79	0.23	0.15
MAP	0.45	0.20	0.18	0.30	0.35	0.02
Correlations for VAI						
Parameters	CG	p	EH	p	Both	p
Age	0.90	< 0.001	0.58	< 0.001	0.67	< 0.001
SBP	0.43	0.22	0.29	0.11	0.43	0.004
DBP	0.51	0.13	–0.001	0.97	0.19	0.21
MAP	0.52	0.13	0.13	0.45	0.32	0.04

It is shown that trends in both groups of patients (normotensive and hypertensive) were similar. The increasing of augmentation index and pulse wave velocity with age was noted. But in the youngest subgroup of hypertensive patients the augmentation index and pulse wave velocity were higher than in their peers with normal blood pressure.

In previously published papers it was pointed on the correlations of AIx and PWV with age, as well as with blood pressure [1, 2]. Therefore, we analysed the association of these parameters. Results of simple correlation presented below (Table II).

All studied parameters of pulse wave showed strong relationship with age, but the relationship of VAI with age was superior in its strength and significance. It was especially strong (r = 0.90) in normotensive patients. Also there was a moderate correlation between all three indicators (AIx, PWV and VAI) with SBP and MAP in the united sample, which included both, hypertensive and normotensive persons. No significant correlation of any of the examined parameters of central pulse wave with DBP was revealed.

Since an augmentation index demonstrated a clear tendency to rise with increasing age, we suggested

Table III. Average values of VAI in the age subgroups of the essential hypertension and the control group.

Subgroup	CG	EH	p
20–44	29.3	54.7	< 0.001
45–64	57.8	69.5	< 0.05
65 >	69.8	83.5	< 0.05

p — significance of difference according to the Mann-Whitney test

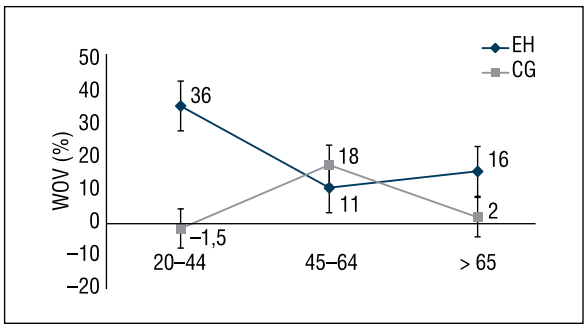

Figure 1. The values of waste of vessels index in different age subgroups of the essential hypertension and the control group

that AIx should be an indicator of vessels age. PWV also had the same tendency. Identified trends are in good agreement with the results of previous studies [1, 2]. Therefore, we proposed to use the product of augmentation index and pulse wave velocity as an integral assessment of the central pulse wave — "vascular age index" (VAI). To avoid negative values of the product, AIx value should be calculated by the formula (2). To simplify the interpretation of the values, the product value should be divided by 20.

The values of VAI obtained in subjects of the control group were approaching to the calendar age and in patients with hypertension — often exceeded it. The results obtained in different age subgroups of both groups are presented in Table III.

According to VAI, the hypertensive patients significantly differed from their peers who did not have hypertension. To quantify the differences in biological and calendar age of vessels we proposed to calculate the index provisionally named as "wearout of vessels" (WOV). The formula is shown below:

wherein:

$$WOV = \frac{VAI - CA}{CA} \times 100\ (\%)\ (3)$$ wherein

VAI — vascular age index determined by the formula (2)

CA — calendar age

Figure 1 demonstrates differences between means of WOV in the correspondent age subgroups of CG and EH.

As it is shown, the average values of WOV in hypertensive patients of the younger age group differ significantly from the corresponding subgroup of control group. At the same time, in the middle and the oldest subgroups differences are statistically non-significant. But means of WOV differed significantly when groups were compared without age subdivision: 4.5 (9.2)% in the control group and 18.2 (8.3)% in hypertensive patients, p = 0,04.

Discussion

Our data confirmed other researchers' findings about the relationship between AIx and PWV on the one hand, and age and blood pressure on the other hand. Also, we have got the evidence that the influence of age on the parameters of central pulse wave was more pronounced in hypertensive patients compared with individuals with normal blood pressure.

It was shown that in patients of 25–44 years pathological changes of central pulse wave parameters could serve as an additional argument for the diagnosis of hypertension. Conclusions of Sharman J.E. *et al.*, 2013, that providing of central pulse wave study can optimize the management plan may be indirect evidence that supports this idea [3].

VAI proposed for evaluation of CPW showed the strong correlation with age. The correlation coefficient was particularly high (up to 0.9) in examined normotensive patients suggesting that VAI corresponded to the biological age of vascular system. Speculating about the possibility of practical rationale of VAI, the results of Anglo-Cardiff Collaborative Trial (ACCT) should be mentioned. The main conclusion of this study was that the AIx was more sensitive marker and risk factor of arterial stiffness in young persons, and PWV — in the elderly [4]. Thus, the use of two indicators simultaneously can improve individual prognosis. Discussing the prediction value of VAI, it is necessary to note that this index is able to change the principle of individual risk assessment. Usually, the routine risk assessment is an estimate of probability of certain event (death, stroke, heart attack). Its interpretation requires a person to be informed of reference and exceeding values. But simple comparison of the biological and calendar age in case of VAI requires no special skills. As we can see, it contributes to better compliance. Comparison of the accuracy assessment of the cardiovascular system made on the basis of AIx75, PWV and VAI showed that VAI was not inferior to the other two options, but it greatly simplified the interpretation of the data.

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